fine granules may be coated, as disclosed on page 23, line 7 – page 26, line 23 of the specification. Therefore, the dependent claims 14-17 do not represent a separate invention.

Applicants respectfully request withdrawal of the withdrawal of claims 14-17 for the reason provided above.

II. Discussion of the Rejection under 35 U.S.C. §103(a)

The rejection of claims 1-7 and 13-19 for obviousness over the Ohno *et al.*, U.S. Patent No. 5,958,453 in view of Shashoua *et al.*, U.S. Patent No. 5,795,909 has been maintained, as the Examiner found the previously submitted Declaration unpersuasive.

The present invention is directed to a rapidly disintegrable solid preparation comprising granules or fine granules of lansoprazole, a sugar and a low-substituted hydroxypropylcellulose having 5% to less than 7% of hydroxypropoxyl groups; a method for preparing a rapidly disintegrable solid preparation as well as a method for improving fast disintegrability of a solid preparation. Applicants do not believe that their invention, as set forth in the present claims, is taught or suggested by the combination of the cited references.

Ohno *et al.* is directed to solid pharmaceutical preparations. Low-substituted hydroxypropyl cellulose is mentioned generally as a disintegrant in col. 5, lines 23-24 of the cited reference. More specifically, L-HPC was utilized in Comparative Examples 3, 4 and 5. However, the cited L-HPC is different from the L-HPC presently claimed. The cited L-HPC is of higher hydroxypropoxyl content, as elaborated upon below.

Applicants now provide evidence, in the form of a Declaration from Dr. Ohno, establishing that the low-substituted hydroxypropyl cellulose (L-HPC) in the Examples of the cited '453 reference had a higher weight percentage of hydroxypropoxyl groups than that of the L-HPC component of the presently claimed solid preparations. In his Declaration, Dr. Ohno (an inventor of cited U.S. Patent No. 5,958,453) avers that the L-HPC which was used in the Examples of the '453 reference had from 10.0% to 12.9% by weight of hydroxypropoxyl groups.

Additionally, Applicants have submitted a further Declaration, of Mr. Watanabe, a Shin Etsu employee familiar with L-HPC products available at the time of the filing of the present application. Shin-Etsu was identified as a source of L-HPC in col. 5, line 24 of the cited reference. Mr. Watanabe's Declaration has been provided to illustrate the point that the L-HPC component of the presently claimed preparations was not commercially available prior to the filing of the present application. Mr. Watanabe's Declaration indicates that the lowest range of

hydroxypropoxyl group content for L-HPC commercially available at the time of filing of the present application was 7.0 –9.9%.

Appendix A, attached to this amendment, further supports Mr. Watanabe's Declaration. It is a copy of a Shin-Etsu catalogue, dated February 1998, as indicated on the last page of the catalogue. On page 14, the hydroxypropoxyl contents of available L-HPC's is indicated. The lowest range available of hydroxypropoxyl group content (7.0 – 9.9%) for L-HPC commercially available at the time was found in Shin-Etsu's commercial products LH-22 and LH-32.

The evidence now provided confirms that the L-HPC component of the presently claimed solid preparations was not known prior to the filing of the present application.

Nor do the Applicants believe that the specific *and lower* hydroxypropoxyl group range for the L-HPC component of the solid preparations presently claimed would be obvious from a reading of reference which utilized a higher hydroxypropoxyl group range for the L-HPC component. This is so since although the *lower* range (7.0 – 9.9 % hydroxypropoxyl group content) L-HPC was commercially available, Ohno elected to utilize L-HPC with a range of 10.0 – 12.9% hydroxypropoxyl group content. Therefore, if any trend were to have been identified by one skilled in the art, it would be that higher hydroxypropoxyl group content in the L-HPC component provided better results; not a lower hydroxypropoxyl group content, as presently claimed. Thus, the provided evidence shows that, if a trend may be identified at all, the reference (using *a higher* range than the lowest commercially available range) actually teaches away from the present invention (using *a lower* range than lowest commercially available range). Therefore, the '453 reference provides no teaching or suggestion of the L-HPC component of the presently claimed preparations and methods.

The deficiencies of Ohno *et al.* are not cured by Shashoua *et al.* The Examiner has indicated previously (Paper No. 7) that the reference '909 has been added for the teaching of active ingredients. However, the cited reference includes lansoprazole only as an agent to be conjugated to DHA, for the specific purposes of the cited reference.

Athough the '909 reference is directed to conjugates of cis-docosahexanoic acid and taxanes, a broader teaching is also provided in the specification that DHA may be conjugated to virtually any drug compound or diagnostic agent, as stated in col. 19, lines 62 and 63 of the cited reference. This broad statement is followed by a laundry list of exemplary compounds which is twenty-seven columns long. Lansoprazole is mentioned among hundreds of other compounds as appropriate conjugates, in col. 44, line 26.

There is no teaching or suggestion of non-conjugated lansoprazole in Shashoua *et al.* Moreover, there is no teaching or suggestion in the cited reference of solid preparations of active ingredients having a sugar and L-HPC, as presently claimed.

In summary, the Ohno *et al.* reference does not disclose the L-HPC component of the presently claimed solid preparations. The Shashoua *et al.* reference does not teach the preparations of the present invention, let alone the active ingredient of the present invention. Therefore the combination of the cited references does not render the present invention obvious.

For this reason, Applicants submit that their invention, as set forth in independent claims 1, 18 and 19 as amended, is neither taught nor suggested by the combination of the cited references. Claims 2-7 and 13-17 depend upon claim 1, so Applicants submit that these more specific dependent claims are also non-obvious. Therefore, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. Sec. 103(a) over Ohno *et al.*, U.S. Patent No. 5,958,453 in view of Shashoua *et al.*, U.S. Patent No. 5,795,909.

III. Previously Submitted Information Disclosure Statement

Applicants submitted an Information Disclosure Statement at the time of the filing of the present application, on October 20, 1999. Four references were cited. Applicants have not yet received an Examiner-initialed copy of their Form 1449. Applicants respectfully request that the Examiner provide the initialed copy, if the references have been reviewed. Applicants respectfully request that the Examiner contact Applicants' attorney if the Form 1449 or any of the references are missing from the Examiner's file.

IV. Conclusion

Reconsideration of the claims as amended in view of the arguments made above is solicited. Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, she is respectfully requested to call Applicants' attorney.

Respectfully submitted,

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